Applicant: T. Keith Blackwell et al. Attorney's Docket No.: 10276-0093US1

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## Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

## Listing of Claims

- 1. (Currently amended) A method for determining whether a test compound is a candidate <u>SKiNhead 1 (SKN-1)</u>-mediated oxidative stress response-activating compound, comprising:
  - (a) providing a first nematode capable of expressing a SKN-1 polypeptide and containing at least one <u>reporter</u> transgene comprising:
    - (i) an oxidative stress resistance gene promoter, wherein the promoter comprises a SKN-1 binding site and is effective at directing SKN-1-induced gene expression, and operably linked to
      - (ii) a reporter gene operably linked to the promoter;
    - (b) contacting the first nematode with the test compound; and
  - (c) determining whether expression of the <u>reporter</u> transgene is increased <u>in the</u> <u>first treated nematode compared to a control nematode not treated with the test</u> <u>compound</u>, wherein an increase in expression of the <u>reporter</u> transgene <u>in the first treated</u> <u>nematode</u> indicates that the test compound is a candidate SKN-1-mediated oxidative stress response-activating compound.
- 2. (Currently amended) The method of claim 1, further comprising determining whether the candidate compound is an inhibitor of GSK-3 enhances SKN-1-mediated expression of an oxidative stress resistance gene in a cell.
- 3. (Currently amended) A method for determining whether a test compound is a candidate SKN-1-mediated oxidative stress response-inhibiting compound, comprising:

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(a) providing a first nematode capable of expressing a SKN-1 polypeptide and containing at least one <u>reporter</u> transgene comprising:

- (i) an oxidative stress resistance gene promoter, wherein the promoter comprises a SKN-1 binding site and is effective at directing SKN-1-induced gene expression, and operably linked to
  - (ii) a reporter gene operably linked to the promoter;
- (b) contacting the first nematode with the test compound;
- (c) before, during, or after step (b), subjecting the nematode to conditions that activate the SKN-1-mediated oxidative stress response in the absence of the test compound; and
- (d) determining whether expression of the <u>reporter</u> transgene is decreased or unchanged <u>in the first treated nematode compared to a control nematode not treated with the test compound</u>, wherein decreased or unchanged expression of the <u>reporter</u> transgene <u>in the first treated nematode</u> indicates that the test compound is a candidate SKN-1-mediated oxidative stress response-inhibiting compound.
- 4. (Currently amended) The method of claim 3, further comprising determining whether the candidate compound is an inhibitor of SKN-1-mediated expression of an oxidative stress resistance gene in a cell.

## 5. - 10. (Cancelled)

11. (Previously presented) The method of claim 1, wherein the promoter is a promoter of a gene encoding a protein selected from the group consisting of:  $\gamma$ -glutamine cysteine synthase heavy chain, glutathione synthetase, NADH quinone oxidoreductase, superoxide dismutase, catalase, and glutathione S-transferase.

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12. (Previously presented) The method of claim 1, wherein the reporter gene is a gene encoding a protein selected from the group consisting of: green fluorescent protein,

chloramphenicol acetyl transferase, ß glucuronidase, and luciferase.

13. (Previously presented) The method of claim 1, wherein the nematode in step (a) is

Caenorhabditis elegans.

14. - 38. (Cancelled)

39. (New) The method of claim 1, wherein the control nematode is the test nematode

before being contacted with the test compound.

40. (New) The method of claim 3, wherein the control nematode is the test nematode

subjected to conditions that activate the SKN-1-mediated oxidative stress response before being

contacted with the test compound.

41. (New) The method of claim 1, wherein the control nematode is a second nematode.

not contacted with the test compound.

42. (New) The method of claim 3, wherein the control nematode is a second nematode.

subjected to the same conditions that activate the SKN-1-mediated oxidative stress response, in

the absence of the test compound.

43. (New) The method of claim 3, wherein the nematode in step (a) is *Caenorhabditis* 

elegans.

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44. (New) The method of claim 1, further comprising determining whether the compound increases NF-E2-related factor 1 (Nrf1)- or Nrf2 mediated expression of an oxidative stress resistance gene in a mammalian cell, as compared to a control cell.

45. (New) The method of claim 3, further comprising determining whether the compound decreases Nrf1- or Nrf2-mediated expression of an oxidative stress resistance gene in a mammalian cell, as compared to a control cell.